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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/497, 422 02/03/00 BERRY

S ARD2914R1

022921  
ALZA CORPORATION  
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INTELLECTUAL PROPERTY DEPARTMENT  
MOUNTAIN VIEW CA 94039-7210

HM12/0705

EXAMINER

FUBARA, B

ART UNIT

PAPER NUMBER

1615

DATE MAILED:

07/05/00

4

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/497,422	BERRY ET AL.
	Examiner	Art Unit
	Blessing M. Fubara	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

1) Responsive to communication(s) filed on \_\_\_\_\_.

2a) This action is FINAL.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4) Claim(s) 1-38 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-38 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) All b) Some \* c) None of the CERTIFIED copies of the priority documents have been:

1. received.

2. received in Application No. (Series Code / Serial Number) \_\_\_\_\_.

3. received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

**Attachment(s)**

15) Notice of References Cited (PTO-892)

16) Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 & 3.

18) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.

19) Notice of Informal Patent Application (PTO-152)

20) Other: \_\_\_\_\_

DETAILED ACTION

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-33 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knepp et al. and Roorda et al. in view of Nuwayser.

Knepp et al. discloses a stable non-aqueous formulation comprising of suspensions of hormones, peptides, polypeptides, proteins, nucleic acids in non-aqueous, anhydrous, aprotic, hydrophobic, non-polar vehicles having low reactivity (abstract, and 6, lines 15-19). The non-aqueous delivery system of Knepp et al. is implantable, ambulatory infusible and injectable device for sustained delivery (page 6, lines 22-24), and is stored at elevated temperature (37°C) for extended time (page 6, lines 24-25). These stable formulations of Knepp et al. are flowable and as such can be shipped and stored at high temperatures or in implantable delivery devices for long term delivery of drug for 1-12 months or longer (page 6, lines 25-28). Knepp et al. teaches that the flowable formulation may optionally include sucrose, sorbitol, raffinose and dextran to reduce the effective hydration; mannitol to modify the processing characteristics of the proteins or nucleic acids; buffers to modify the pH; and non-ionic surfactants to protect the surface and solubilize the protein or nucleic acid (page 17, lines 19-30). According to Knepp et al., the powdered flowable formulation is uniformly dispersed in anhydrous, non-polar, aprotic, hydrophobic, or low-reactivity vehicle (page 7, lines 23-24) such as mineral oil (page 8, line 27),

and in example 3, page 23, Knepp et al. describes the suspension of plasma protein powder in perfluorodecalin or methoxyflurane vehicles.

Roorda et al. discloses a controlled or sustained release drug delivery system (column 1, lines 5-8), and teaches a viscous controlled release liquid formulation comprising dispersing biologically active particles in high viscosity liquid or semi-liquid. Roorda et al. discloses that the beneficial particles are uniformly distributed and maintained in place at the area in which the formulation is applied by the highly viscous liquid. Roorda et al. teaches formulating the viscous vehicle from dry materials and this is possible because of the fluid nature of the carrier. See column 3, lines 10-20. The viscous liquid of Roorda et al. includes aqueous solution, non-aqueous solution and undiluted non-aqueous liquids (column 3, lines 50-55). The viscous vehicle of Roorda et al. comprises polyvinylpyrrolidone, polyvinyl alcohol, polyethylene glycol (column 4, lines 5-15), polylactic/glycolic acid, PLGA (column 9, example 1), and polyalcohols such as sorbitol (column 6, line 30-31). Roorda et al. suggests that one can control the rate of release of the biologically effective agent by varying the size of the particles, and this affords one to achieve a desired release rate for a particular application (column 3, lines 32-35). Therefore, one can select the size of the particle that will result in the desired release rate, be it for over a period of two or more days (column 3, lines 35-40). The concentration of the polymer is not critical to Roorda et al. who teaches that the concentration of the polymer affects the viscosity of the vehicle such that a polymer concentration is selected to achieve the desired viscosity (column 4, lines 24-34). Roorda et al. recommends the viscosity of the vehicle to range from 10 to about 2,00,000 centipoise, cautions that the viscosity will be different for different applications and polymer and particle concentration affect the viscosity (column 4, lines 41-64). Roorda et al.

further teaches that the biologically effective agent comprises from about 1-60% of the weight of the particles (column 6, lines 49-51), and the biologically effective agents are antibacterial, antiviral, anti-inflammatory and tissue regeneration agents, and local anesthetics (column 5, lines 33-44).

Nuwayser discloses a sustained release transdermal composition having a zero order release of drugs to designated skin are of the user (title and abstract). The drug material of Nuwayser comprises antibiotics, antibacterial agents, hormones, and steroids (column 10, lines 23-30). Nuwayser teaches a viscous delivery vehicle (column 5, line 28) comprising of biodegradable polylactide polymer (column 10, lines 20-23) and glycerol for zero order release of drug microparticles uniformly dispersed and suspended in the viscous liquid (claims 1-10).

Kneppe et al. is silent on the viscosity of the vehicles in which the flowable powder formulation of proteins, hormones and peptides. Nuwayser teaches viscous delivery vehicle comprising of biodegradable polymer for the sustained release of uniformly dispersed and suspended microparticles of hormones, steroids and antibacterial agents. Roorda et al. teaches that the viscosity of the vehicle is controlled by the concentration of the polymer and biologically effective particles. Roorda et al. also teaches that the particle size influences the release rate of the particles from the vehicle. Roorda et al. suggests that one can select a particle size to achieve a desired release rate, and polymer and particle concentration for the desired vehicle viscosity. See the preceding paragraphs for the discussions.

The expected result is a non-aqueous uniform bio-compatible viscous delivery vehicle for suspending and delivering beneficial agents at a release rate that is determined by the choice of particle size. Therefore, it would have been obvious to one having ordinary skill in the art at

the time the invention was made to use the teachings of Knepp *et al.* and Roorda *et al.* in the manner taught by Nuwayser. One having ordinary skill in this art would have been motivated to select polymer and polymer concentration to build a non-aqueous homogeneous bio-compatible viscous delivery vehicle that has the required viscosity for the desired application, and choose a stable flowable biologically effective agent having the appropriate particle size for suspension and delivery from the viscous vehicle. The burden is on the applicant to demonstrate the criticality of the slow flow rate and the exit shear rate of  $1 \times 10^{-7}$  reciprocal second. Knepp *et al.* (page 14, lines 11) teaches that it is normal practice to include ascorbic acid, anti-oxidant in dilute aqueous peptide and protein formulations and also that formulation of dry protein or nucleic acid powders is well known in the art (page 17, line 30). It is therefore *prima facie* obvious to include anti-oxidant in the formulation.

Claim 34 is objected to because it depends for a rejected claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is 703-308-8374. The examiner can normally be reached on Monday to Friday from 7 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

THURMAN K. PAGE  
SUPPLYING PATENT EXAMINER  
TECHNOLOGY CENTER 1600

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Art Unit: 1615

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